UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,886	10/19/2004	Gihad Dargazanli	SSL0064	6340

5487 7590 07/25/2006

ROSS J. OEHLER
SANOFI-AVENTSI U.S. LLC
1041 ROUTE 202-206
MAIL CODE: D303A
BRIDGEWATER, NJ 08807

EXAMINER	
PERLINGER, SARAH E	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/511,886	DARGAZANLI ET AL.	
	Examiner	Art Unit	
	Sarah E. Perlinger	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-11 and 17-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *6,7,10,11 and 19-21* is/are allowed.

6)☒ Claim(s) *1-3,5,8,9,17,18 and 22-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-3, 5-11, 17-38 are pending. Claims 12-16 were canceled and claims 17-38 were added in the amendment filed May 17, 2006.

2. ***Oath/Declaration***

The oath filed on May 17, 2006 is in compliance with 37 CFR 1.67(a). Therefore, the objection to the oath has been withdrawn.

3. ***Specification***

The instructions Applicants provided with regard to the objections to the specification and abstract will be followed at the time of issuance. At that time the objections will be obviated.

4. ***Claim Rejections - 35 USC § 112***

Applicant's argument, see page 12 of 20, filed May 17, 2006, with respect to the 112, Second paragraph rejection against claims 1-3, 5, 8-9 and 12-14 has been fully considered and are persuasive. The 112 Second paragraph rejection of claims 1-3, 5, 8-9 and 12-14 has been withdrawn.

5. In view of the cancellation of claims 12-16 in the amendment filed May 17, 2006, the 112 second paragraph rejection of claims 12-16 has been withdrawn.

6. In view of the cancellation of claims 12-16 in the amendment filed May 17, 2006, the 112 first paragraph rejections (both written description and enablement) have been withdrawn.

7. ***Claim Rejections - 35 USC § 103***

Applicant's arguments, see Response, filed May 17, 2006, with respect to the 103(a) rejection against claims 1-3 and 5-11 have been fully considered and are persuasive. The 103(a) rejection of claims 1-3 and 5-11 has been withdrawn.

8. ***Double Patenting***

In the response filed May 17, 2006 regarding the provisional obviousness-type double patenting rejection of claims 1-3, 5, 8-9 and 12-14 over claims 1-7 of copending Application No. 11/045247, Applicants stated, "..since this is a provisional rejection, upon allowance of either or both of the subject applications a terminal disclaimer will be filed." Since no terminal disclaimer has been filed at this time, the provisional obviousness-type double patenting rejection of claims 1-3, 5, 8-9 and 12-14 over claims 1-7 of copending Application No. 11/045247 is maintained.

The following rejections are necessitated by the amendment of the claims filed on May 17, 2006:

9. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims are indefinite where a method for the treatment of a disorder "associated with" glyt1 or glyt2 is claimed. It is unclear how a disorder would be associated with glyt1 or glyt2 glycine transporters and therefore the scope of the disorders to be treated cannot be ascertained. The instant claims are rendered indefinite because of the vague terminology used.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the

application was filed, had possession of the claimed invention. The instant claim is drawn to a compound according to claim 1 wherein A represents a group of general formula N-R1 in which R1 represents either a hydrogen atom, or a linear or branched (C1-C7) alkyl group optionally substituted with one or more fluorine atoms and said compound is in the form of a free base or of an addition salt with acid. Upon reviewing the specification, description of the instant claimed compound could not be found. The amendment of the claim 17 represents NEW MATTER. This is a NEW MATTER rejection. Removal of the new matter is required see *In re Rasmussen*, 211 USPQ 323.

11. Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The instant claim is drawn to several species of the compound according to claim 1. While written description for threo-2-chloro-N-[(1-ethylpiperidin-2-yl)phenylmethyl]-3-trifluoromethylbenzamide hydrochloride, (Specification, page 15, compound no. 33) 2-chloro-N-[(1S)-[(2S)-1-methylpiperidin-2-yl)phenylmethyl]-3-trifluoromethyl]-benzamide hydrochloride, (Specification, page 16, compound 18) threo-4-Amino-3-chloro-n-[(1-methylpiperidin-2-yl)phenylmethyl]-5-trifluoromethylbenzamide hydrochloride, (Specification, page 20, compound 24) 4-Amino-3-chloro-N-[(1R)-[(2R)-1-methylpiperidin-2-yl] phenylmethyl]-5-trif- luoromethylbenzamide hydrochloride, (Specification, page 24, compound 25) threo-2-Chloro-N-[phenyl(piperidin-2-yl)methyl]-3-trifluoromethylbenzamide hydrochloride, (Specification, page 25) has been provided in the specification, written description for threo-2-chloro-N-[(1-ethylpiperidin-2-yl)phenylmethyl]-3-trifluoromethylbenzamide, 2-chloro-N-[(1S)-[(2S)-1-methylpiperidin-2-yl)phenylmethyl]-3-trifluoromethyl]-benzamide, threo-4-Amino-3-chloro-n-[(1-methylpiperidin-2-yl)phenylmethyl]-5-trifluoromethylbenzamide, 4-Amino-3-chloro-N-[(1R)-[(2R)-1-methylpiperidin-2-yl] phenylmethyl]-5-trif- luoromethylbenzamide, threo-2-Chloro-N-

[phenyl(piperidin-2-yl)methyl]-3-trifluoromethylbenzamide has not been found in the specification. Though the hydrochloride salt forms of the aforementioned compounds were found in the specification, the compounds were not found in the specification. The amendment of the claim represents NEW MATTER. This is a NEW MATTER rejection. Removal of the new matter is required see *In re Rasmussen*, 211 USPQ 323.

12. Claims 22-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Upon review of the specification, written description of a pharmaceutical composition comprising a compound according to claim 18, 19, 20 or 21 combined with an excipient could not be found. The amendment of the claims 22-25 represents NEW MATTER. This is a NEW MATTER rejection. Removal of the new matter is required see *In re Rasmussen*, 211 USPQ 323.

13. Claims 30-34, 36-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to a method for the treatment of a disorder associated with a glyt1 or glyt2 glycine transporter comprising administering to a patient in need of said treatment an effective amount of a compound according to claim 17, 18, 19, 20 or 21. Upon review of the specification, written description of the aforementioned methods could not be found. The amendment of the claims 30-34, 36-38 represents NEW MATTER. This is a NEW MATTER rejection. Removal of the new matter is required, see *In re Rasmussen*, 211 USPQ 323.

14. The rejection of claims 12-16 under 35 U.S.C. 112 first paragraph is maintained for the newly replaced claims 26-38. The same rationale is repeated for the newly replaced claims 26-38.

Claims 26-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The scope of the claims is drawn to a method of treating a disorder associated with glyt1 or glyt2 glycine transporters, which broadly encompassed both post synaptic inhibitory and excitatory amino acid neurotransmission (see Lopez-Corcuera supra). No description was found for any compound to have contradictory inhibitory and excitatory activity in the specification.

Claims 26-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01(a) "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." The factors to be considered herein are those set forth as the In re Wands, 8 USPQ 2nd 1400 (1988) decision.

Nature of Invention

The claims are drawn to a method for the treatment of a disorder associated with glycine transporters.

Scope of the Claims

The scope of the claims are drawn to a method for the treatment of a disorder associated with glyt1 or glyt2 glycine transporters, which broadly encompasses both post synaptic inhibition and excitatory amino

acid neurotransmission (see Lopez-Corcuera supra). No description was found for any compound to have contradictory inhibitory and excitatory activity in the specification.

The State of the art and Predictability

The state of the art in CNS intervention is highly unpredictable. The blood brain barrier protects the central nervous system from pathogenic organisms, toxic molecules, and even its own immune system. This barrier also prevents entry of possible therapeutic molecules into the brain. Presently, little is known about the molecular mechanisms that control the blood brain barrier (Daneman et al., *Cell*, 2005, 123, 9-12). Water-soluble materials that would ordinarily be taken up in the body, will not pass through the blood brain barrier causing drug delivery to the CNS to be an extremely difficult task (LeBowitz, *PNAS,* 2005, 102, 14485-14486).

The amount of guidance and working examples

The specification is limited to a description of *in vitro* and *ex vivo* activity. The Specification (pages 39-45) describes *in vitro* and *ex vivo* generic compounds' inhibition of the capture of glycine, by glycine transporters. *In vitro* and *ex vivo* measurement in synaptic glycine re-uptake does not support such contradictory scope of the claims. In addition, *in vitro* and *ex vivo* measurements, although providing screening for leading compounds, does not provide description or enablement for CNS therapy for which factual evidence of passing the blood brain barrier, dosage, and site of administration, must be made known to one having ordinary skill in the art to practice such method. Section 112 requires the application itself to inform, not for others to fine out by themselves. Ex parte Aggarwal 23 USPQ 2nd 1481. In re Gardner 166 USPQ 138.

In view of the highly unpredictable state of the art in CNS intervention and the lack of any description of the instant claimed compound having any ability to treat any pathology or symptom, or any pathology or symptom being inexorably linked to inhibition of a glycine transporter at any specific IC_{50}, one

of ordinary skill in the art would not be able to use the instant claimed compounds in the instant claimed methods.

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. ***Allowable Subject Matter***

Claims 6-7, 10-11, 19-21 are allowed. The instant claims are allowed because the prior art did not teach or suggest the instant benzamide compounds or salts in the (1R,2R) or (1S,2S) enantiomer form wherein the phenyl group of the benzamide moiety is substituted with a trifluoromethyl group.

17. ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Sarah E. Perlinger, whose telephone number is (571) 272-5574. The examiner can normally be reached on Monday through Friday, 8:30 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Thomas McKenzie, can be reached at (571) 272-0670. The fax number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DP

07/12/2006

Celia Chang
Primary Examiner
Art Unit 1625